REMARKS

Claims 1, 2, 4, 7, 8, 27-29, 31, 41, and 42 have been rejected under 35 U.S.C. § 103(a) as obvious over U.S. Patent Publication No. 2003/0064099 (Oshlack) in view of DOW Technical Data, POLYOX™ WSR (Dow).

According to the Examiner, Oshlack discloses a sustained release dosage form comprising (a) oxycodone, (b) an aversive agent/gelling agent, such as polyethylene oxide (PEO), and (c) waxes. Further, according to the Examiner, the PEO may be present in tablets in a ratio to the opioid agonist of from about 1:15 to about 15:1 by weight, which encompasses the instant claim limitation that the synthetic or natural polymer is present in an amount sufficient to result in a breaking strength of at least 500N. The Examiner contends that the melt-extrusion technique disclosed in Oshlack encompasses the sintering technique recited in the instant claims. The Examiner acknowledges that Oshlack does not disclose a PEO molecular weight of 1-15 million and a dosage form having a breaking strength of at least 500N.

According to the Examiner, Dow discloses the use of high molecular weight POLYOX™ WSR for sustained release solid dosage forms, which "are excellent choices for melt processing." Office Action, p. 5. The Examiner contends that it would have been obvious to use POLYOX™ WSR in an amount sufficient to result in a breaking strength of at least 500N for the sustained release dosage form of Oshlack because both disclosures are directed to sustained release forms containing PEO polymers in thermoformed tablets. *Id.* at 5-6. Applicants respectfully traverse this rejection on the following grounds, each of which, independently or combined, is a basis for withdrawing the rejection.

I. Prior art must be considered as a whole

A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984); MPEP 2141.02.

When read as a whole, Oshlack discloses:

- "[A]n oral dosage form comprising an opioid analgesic; and at least one aversive agent for reducing the abuse of the opioid analgesic." Oshlack, para. 19;
- The object of such a dosage form is to decrease parenteral abuse. See, e.g., Oshlack, para. 13;
- The aversive agent can be a bittering agent, a gelling agent, an irritant, or a combinations thereof that is released when the dosage form is tampered with.
- "Tampering" includes crushing, grinding, and chewing. Oshlack, para. 31. The aversive agent is not released when the dosage form is administered as directed, e.g., a tablet is swallowed intact. See, e.g., Oshlack, paras. 21-25, 27, 30 38-40.

Dow discloses that POLYOX WSR polymers are well-suited to thermoplastic processing and can be processed into various solid dosage forms which exhibit sustained release. Dow, p. 3. The polymers are available in molecular weights ranging from 100,000 to 7,000,000 amu. Dow, p. 1. Dow discloses that the low molecular weight grades have good flow characteristics and can be processed using conventional equipment. The high molecular weight grades have limited melt flow and often require plasticizer. Dow, p. 1.

Thus, when read as a whole, Oshlack discloses an oral, sustained release opioid dosage form with reduced parenteral abuse based on an aversive agent that is released when the dosage form is tampered with, i.e., crushed, ground or chewed. When read as a whole, Dow discloses that POLYOX WSR polymers may be used in sustained

release dosage forms. No combination of the references discloses or suggests the desirability of a dosage form having a breaking strength of at least 500N, which would defeat the purpose of including an aversive agent according to Oshlack.

II. There is no prima facie obviousness because the proposed prior art modification would change the principle of operation of the prior art

If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious. MPEP 2143.01. The principle of operation in Oshlack is that abuse will be reduced because an aversive agent is released from the dosage form when it is tampered with, e.g., crushed, ground or chewed. A dosage form modified to meet the at least 500N breaking strength limitation of the instant claims cannot be tampered with in this manner and, therefore, Oshlack's principle of operation would be defeated.. See, specification, para. 8-9.

In re Ratti is instructive. In that case, the primary reference taught a device that required rigidity for operation, whereas the claimed invention required resiliency. The court reversed the rejection, holding that the "suggested combination of references would require ... a change in the basic principle under which the [primary reference] construction was designed to operate." See, *In re Ratti*, 270 F.2d 810, 813, 123 USPQ 349, 352 (CCPA 1959). Here, the prior art requires tampering by chewing, crushing or grinding for its operation, whereas the claimed invention requires a breaking strength which precludes such tampering.

For the reasons stated above, this rejection should be withdrawn because the Examiner's proposed modification would change the primary prior art reference's principle of operation.

III. Impermissible hindsight

Hindsight reasoning is not permissible when it relies on knowledge "gleaned only from [the] applicant's disclosure..." *In re McLaughlin* 443 F.2d 1392, 1395, 170 USPQ

209, 212 (CCPA 1971); MPEP 2145. The desirability of a breaking strength of at least 500N is only gleaned from the instant specification, which discloses that a breaking strength of at least 500N can prevent tampering with an oral dosage form by pulverization and, in so doing, reduce abuse. See, e.g., specification, para. 8-9. Oshlack does not provide this teaching – quite the opposite, Oshlack teaches a dosage form that can be pulverized (i.e., crushed, ground, or chewed). Dow does not provide the missing teaching. The Examiner's proposed modification to the prior art is based upon the teaching of the instant application. Accordingly, this rejection should be withdrawn.

IV. Numerous parameters, no guidance

According to the Federal Circuit, "obvious to try" does not render a claim obvious when:

> what would have been 'obvious to try' would have been ... [to] try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful.

In re Kubin, 561 F.3d 1351, 1359, 90 USPQ 2d 1417 (Fed. Cir. 2009) (quoting *In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988)).

Here, one of ordinary skill in the art would have had to try each of the at least 40 "gelling agent" genera and species (including PEO) disclosed in Oshlack to arrive at the claimed polymer/opioid combination (Dow does not disclose opioids). Further, to arrive at the claimed dosage form, one of ordinary skill in the art would have had to try PEO's with molecular weights between 100,000 to 7,000,000 amu (disclosed in Dow, Oshlack does not disclose PEO molecular weights), and select the proper amount of the high molecular weight PEO from a range of 1:40 to about 40:1 by weight of PEO to opioid (broadest range disclose in Oshlack) or, for the sake of argument, about 1:15 to about 15:1 (narrower range in Oshlack, cited by the Examiner), to result in a breaking strength of at least 500N.

Further, the prior art does not indicate that the selection of gelling agent is critical and, in fact, discloses that xanthan gum and pectin are preferred, not PEO. Oshlack, para. 49. The direction provided by Oshlack is *away* from the instantly claimed dosage form having a breaking strength of 500N because Oshlack is directed to a dosage form that *can* be crushed, ground, or chewed. If one of ordinary skill in the art did try PEO, Dow guides one of ordinary skill in the art toward choosing a low molecular weight PEO because, unlike the high molecular weight PEO's, they have good flow characteristics and can be processed using conventional equipment. Dow, p. 1.

No combination of the prior art provides any indication or direction to try a certain polymer, at a certain molecular weight, in a certain amount to arrive at a dosage form having a breaking strength of 500N. Further, no combination of the references provides any indication or direction that such a breaking strength would have been desirable. Under the Federal Circuit's post-*KSR* holding in *In re Kubin*, this rejection should be withdrawn.

IV. A possibly inherent property of a hypothetical compound does not render a claim obvious

According to the Examiner, "it would have been obvious to one ordinarily skilled in the art that the sustained release dosage forms of the combined references of [Oshlack and Dow] contains a high molecular weight PEO polymer in an amount sufficient to result in a breaking strength of at least 500N. If the prior art teaches the composition, then the properties are also taught by the prior art." Office Action, p. 6. Thus, the Examiner contends that, if the various parameters were combined in such a way, as to arrive at the instantly claimed compound (contrary to the guidance provided in the prior art), the resulting composition would necessarily possess the teaching missing in the prior art, i.e., the breaking strength limitation.

As stated in the sections above, no combination of the references discloses or suggests an opioid dosage form according to the instant claims having a breaking strength of at least 500N. Claims are not rendered obvious by recognizing an advantage of the dosage form (the claimed breaking strength) disclosed in the instant

specification, and working backward to piece together prior art to arrive at the dosage form. "[A] retrospective view of inherency is not a substitute for some teaching or suggestion supporting an obviousness rejection." *In re Rijckaert*, 891 F.2d 899, 901, 12 USPQ 1248, 1250 (Fed. Cir. 1989). The combined prior art does not disclose or suggest a dosage form having a breaking strength of at least 500N. "[T]he inherency of an advantage and its obviousness are entirely different questions. That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown." *In re Spormann*, 363 F.2d 444, 448, 150 USPQ 449 (CCPA 1966). The instantly claimed sintered, controlled release dosage form having an opiate or opioid active agent, and at least one synthetic natural polymer comprising a polyalkylene oxide having a molecular weight of 1-15 million, present in an amount sufficient to result in a breaking strength of at least 500N was unknown.

The Examiner contends that if Oshlack and Dow are combined to arrive at the instant invention then the breaking strength limitation is inherent in this hypothetical compound. Citing *In re Spada* for support, the Examiner states that: "[i]f the prior art teaches the composition, then the properties are also taught by the prior art." Office Action, p. 6. Further, the Examiner states that the: "burden is shifted to Applicant to show that the prior art product does not possess or render obvious ... the instantly claimed product ..." *Id*.

In re Spada is an anticipation case where the composition was actually disclosed in the prior art. Here, the Examiner pieces together prior art references in an obviousness rejection to arrive at the instant invention, and then requires the Applicant to distinguish the invention from itself. This approach was rejected by Judge Rich and the CCPA in *In re Chapman*, 357 F.2d 418 (CCPA 1966). The claims at issue in *Chapman* related to methods for chlorinating polyethylene resins. The primary reference disclosed the claimed process except that it used low molecular weight polyethylene instead of high molecular weight polyethylene. The Examiner in *Chapman* stated that it would have been obvious to replace the low molecular weight polyethylene with high molecular weight polyethylene based on a secondary reference. On appeal, the Board stated that such a substitution would inherently yield a product substantially the same as that claimed. The Board faulted the applicant's declaration for not

comparing the hypothetical compound to the claimed invention. The Court rejected the Board's approach, stating that this "would amount to requiring comparison of the results of the invention with the results of the invention."

The comparison required by the Federal Circuit is that "[w]hen an obviousness rejection is based on a combination of the prior art references, the comparison need only be between the closest prior art reference and the claimed invention." *In re Baxter Travenol Labs*., 952 F.2d 388, 392 (Fed. Cir. 1991). Here, the closest prior art is Oshlack. Oshlack discloses an oral pharmaceutical composition that includes an aversive agent in order to reduce abuse when the composition is chewed, ground, or crushed. For the reasons stated above, the instant claims, directed to an oral pharmaceutical composition that cannot be chewed, ground, or crushed (except, perhaps, by extraordinary means) are non-obvious over Oshlack. Thus, this rejection should be withdrawn.

In view of the present amendments and remarks it is believed that claims 1, 2, 4, 7, 8, 27-29, 31, 41 and 42 are now in condition for allowance. Reconsideration of said claims by the Examiner is respectfully requested and the allowance thereof is courteously solicited.

CONDITIONAL PETITION FOR EXTENSION OF TIME

If any extension of time for this response is required, Applicants request that this be considered a petition therefor. Please charge the required petition fee to Deposit Account No. 14-1263.

ADDITIONAL FEE

Please charge any insufficiency of fee or credit any excess to Deposit Account No. 14-1263.

Respectfully submitted,
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